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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/045,732	03/20/98	FULLER C	233/127

022249
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HM22/1007

EXAMINER	
SIU,S	
ART UNIT	**PAPER NUMBER**
1653	7

DATE MAILED: 10/07/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/045,732	Fuller et al
Examiner	**Group Art Unit**
Stephen Siu	1653

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-19 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-19 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The information disclosure statement filed March 20, 1998 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56© most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein with respect to WO/PCT #94/22892 and WO/PCT #93/09127 has not been considered.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

3. Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given **as well as its use**, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary.

Revision of the content of the abstract is required on a separate sheet.

Claim Objections

4. Claims 10, 12, 16, 18 are objected to because of the following informalities: Claim 10, line 13, describes the compound "deoxyguonosine" and claim 12, line 1, describes the compound "deoxyguanisine". Both terms are misspelled. Claim 16, line 4, duplicates the word "is" and claim 18, line 4, duplicates the word "wherein". Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. "Propyl-7-deaza-2'-deoxyguanosine" in Claim 11 is not described in the specification which instead describes "7-propyl-7-deaza-2'-deoxyguanosine".

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 describes a "compound" of formula (II) and differs from claim 5 which describes a "molecule comprising the moiety" of formula (II). Likewise, claim 18 describes a "compound" of formula (II) and differs from claim 6 which describes a "molecule comprising the moiety" of formula (II). Claims 17 and 18 taken in context are confusing as they bear no discernible difference with claims 5 and 6, respectively.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-4, 7-11, 13, 15-16, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Gilead Sciences, Inc (PCT publication W0 93/09127). This reference teaches on page 7 a chemical analog (analog II) of the same structure as the molecule of formula II or molecule of formula III disclosed in the instant invention. The R5 group of analog II corresponds to the R1 group of the molecule of formula II and the R3 group of the molecule of formula III in which the R5 group of analog II described by Gilead Sciences is H, lower alkyl (1-4C), CN, Br, Cl, F, CONR2, lower alkenyl (1-4C) or lower alkynyl (1-4C). The R1 group of the molecule of

formula II recited in the claimed molecule is a C_{1-10} alkyl group optionally substituted by hydroxyl, amino, C_{1-4} alkoxy or halo as recited in Claim 1, for example. Likewise, the R3 group of the molecule of formula III is a C_{2-10} alkynyl group as recited in Claim 19, for example. Analog II disclosed by Gilead Sciences, Inc. anticipates the molecule of formula II in the present invention as, for example, a C_4 alkyl substituted as R5 in analog II would anticipate such a molecule with a like alkyl substituted for R1 in the molecule of formula II or a C4 alkynyl substituted as R3 in the molecule of formula III in the present invention. Furthermore, analog II disclosed by Gilead Sciences encompasses the claimed molecules of both claim 10 and 11 in the present invention, R5 being an ethyl group or propyl group, respectively. Also, Gilead Sciences discloses the incorporation of analogs of structural formula II, wherein R5 is hereinbefore described, into oligomers designed for triple-helix formation with a comlementary duplex DNA strand thus anticipating claim 16 in which the base of the same structure as that described by Gilead is used in a deoxyribonucleic acid sequence.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-4, 7-13, 15-16 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences in view of Li and in further view of Seela and Thomas.

Gilead Sciences, Inc. disclose a chemical analog (analog II) of the same structure as the molecule of formula II or molecule of formula III disclosed in the claimed invention wherein the R5 group of analog II corresponds to the R1 group of the molecule of formula II and the R3 group of the molecule of formula III. The R5 group of analog II described by Gilead Sciences is H, lower alkyl (1-4C), CN, Br, Cl, F, CONR2, lower alkenyl (1-4C) or lower alkynyl (1-4C).

Gilead Sciences does not disclose the molecule wherein the R5 group is a higher alkyl C(5-10).

Li discloses a method of resolving band compression on electrophoretic bands by substituting a purine base with an analog and destabilization of the oligonucleotide. Li discloses improvement in band compression would be accomplished by substituting with N4-methyl-dCTP, prior studies done using 7-deaza-dGTP analogs, and further suggests the use of other N4-alkyl cytosine analogues. Li also suggested the use of more bulky alkyl groups although stating the possibility of the potential limiting factor of false stops.

Li does not disclose further motivation for further substitutions on purine or pyrimidine bases.

Seela and Thomas disclose a method of stabilization of DNA through substitutions on pyrimidine bases with methyl groups. Seela and Thomas state that small pyrimidine 5-substituents have steric freedom in the major groove of B-DNA but that if their size is increased, then

structural changes occur to decrease the Tm and hence their stability. Seela and Thomas further teach a similar situation in 7-substituted 7-deazapurines.

One of ordinary skill in the art would have been motivated to utilize a substituent larger than a methyl group on a 7-substituted 7-deazapurine because the compound previously disclosed by Gilead Sciences uses a C(1-4) substituent while Li taught the substitution of a methyl group in the resolution of compression artifact on electrophoretic gels while suggesting the use of larger groups despite potential problems with false stops. Further, as per teachings of Seela and Thomas, oligonucleotide stability is decreased with substitutions on pyrimidine bases with methyl groups and if the size of the pyrimidine substituents is increased then steric freedom in the major groove of B-DNA is hindered and stability would decrease. Seela and Thomas also stated that this principle is applicable to 7-substituted 7-deazapurines. Therefore, it would have been *prima facie* obvious, motivated by resolving band compression of electrophoretic bands, to perform the teachings of Li on the analog of Gilead Sciences by substitution of bases and substituting larger groups on 7-substituted 7-deazapurines to increase instability of the oligonucleotide as per the teachings of Seela and Thomas.

Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art to have practiced the claimed invention.

13. Claim 5 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences, Inc in view of Stryer, Lubert; Biochemistry, 3rd Ed., 1988, W.H. Freeman & Co., New York.

Gilead Sciences discloses a nucleoside/nucleotide molecule for incorporation into oligomers designed for triple-helix formation with a complementary duplex DNA strand wherein R5 (corresponding to R1 in the present application) may be a C_{1-4} alkyl.

Gilead Sciences does not demonstrate the use of said molecule in a method for determining the nucleotide base sequence of a DNA molecule.

Stryer discloses methods of DNA sequencing using nucleotides.

One of ordinary skill in the art would have been motivated to apply the nucleotide of Gilead Sciences in DNA sequencing because said nucleotide was known in the art through the teachings of Gilead Sciences and use of nucleotides in DNA sequencing was also known in the art through the teachings of Stryer.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art to have performed the claimed method with the claimed molecule.

14. Claims 6 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences in view of Mathews, Christopher; Biochemistry, Benjamin/Cummings Publishing Company, Inc., 1990.

Gilead Sciences discloses a nucleoside/nucleotide molecule for incorporation into oligomers designed for triple-helix formation with a complementary duplex DNA strand wherein R5 (corresponding to R1 in the present application) may be a C_{1-4} alkyl.

Gilead Sciences does not demonstrate the method of elongation of an oligonucleotide sequence.

Mathews discloses the method of polynucleotide chain elongation with DNA polymerase and nucleotides.

One of ordinary skill in the art would have been motivated to apply the nucleotide of Gilead Sciences in the elongation of an oligonucleotide sequence because the nucleotide was known in the art through the teachings of Gilead Sciences who also suggested the incorporation of said nucleotides into polynucleotides and polynucleotide chain elongation procedures were known in the art through the teachings of Mathews.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art to have performed the claimed method with the claimed molecule.

15. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gilead Sciences, Inc. in view of Carey, Francis A., Organic Chemistry, 2nd Edition, McGraw Hill, 1992 .

Gilead Sciences, Inc. discloses a nucleoside/nucleotide molecule for incorporation into oligomers designed for triple-helix formation with a complementary duplex DNA strand wherein R5, corresponding to R1 in the claimed molecule (II) and R3 in the claimed molecule (III), is a C_{1-4} alkyl or C_{2-10} alkynyl group, respectively. Gilead Sciences further discloses a synthesis method for said molecule using a "suitably protected nucleotide" (page 22, line 6 and 15).

Gilead Sciences does not disclose the distinct process for the preparation of the molecule (II).

Carey discloses the concepts of protection groups and reduction in the synthesis of organic compounds.

One of ordinary skill in the art would have been motivated to apply organic chemistry principles as set forth by Cary to synthesize molecule II disclosed by Gilead Sciences wherein R5 is a lower alkyl (1-4C) from molecule II disclosed by Gilead Sciences wherein R5 is a lower alkynyl (1-4C) because the molecule was known in the art through the teachings of Gilead Sciences and synthesis steps were also known in the art through the teachings of Carey. It would have been *prima facie* obvious to rely on the synthesis methods set forth by Carey to synthesize the molecule of Gilead Sciences.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art to have performed the synthesis process of the claimed invention to synthesize the molecule of the claimed invention..

Conclusion

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Siu whose telephone number is (703) 308-7522.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bradley Sisson, can be reached at (703) 308-3978.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Correspondence related to this application may be submitted to Group 1653 by facsimile transmission. This faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). **Official communications should be directed to the Technology Center 1600 fax number (703) 308-4242.** Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

Stephen Siu

Patent Examiner

KENNETH R. HORLICK
PRIMARY EXAMINER
GROUP ~~1800~~ 1600 9/30/99

Kenneth R. Horlick, Ph.D.